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**PATENT**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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| In the **PATENT APPLICATION** of: | | | |
| | Gordon Lowe | | |
| **Application No.:** | Not Yet Known | Our File: | JAK-PT002.1 |
| **Filed:** | Not Yet Known | Date: | August 17, 2001 |
| For: CHIRAL PEPTIDE NUCLEIC ACIDS | | | |
| Group: | Not Yet Known | | |
| Examiner: | Not Yet Known | | |

# PRELIMINARY AMENDMENT

BOX PATENT APPLICATION
Commissioner for Patents
Washington, D.C. 20231

Sir:

Prior to examination, Applicant respectfully requests that the application be amended as follows:

## IN THE SPECIFICATION

On page 1, following the Title, please insert the following new paragraph:

--CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a divisional of U.S. Application No. 09/284,179, filed on April 9, 1999, which is a §371 national application of International Application No. PCT/GB97/02820, filed on October 13, 1997.--

At pages 17-18, please replace the paragraph starting at line 29 on page 17 with the following replacement paragraph:

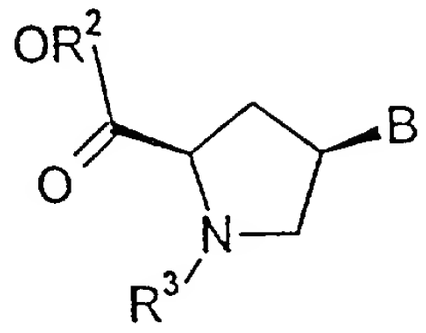
All four bases found in DNA were introduced into the glycylproline building units with the *cis*-D configuration and from these mixed cPNAs containing all four nucleobases have been made. The sequence GTAGATCACT, capped at its C-terminus with L-lysinamide was synthesized, and its binding properties with oligonucleotides investigated. Since it is important to determine the preferred orientation of binding of these novel CPNAs to oligonucleotides, both of the possible complementary oligonucleotides were prepared, *i.e.* Sequence ID No. 2, and Sequence ID No. 3, and hybridised with the chiral PNA. Their $T_m$ values were 47°C and 43°C respectively indicating that the N-terminus of the cPNA preferentially binds to the 5'-terminus of the olignucleotide, and the C-terminus to the 3'-terminus of the oligonucelotide. This is known as the antiparallel mode of binding, but it is seen that the stability of the alternative parallel binding complex is only slightly less stable.

## IN THE CLAIMS

Please cancel claims 1-14 and 19.

Please amend the claims as follows:

15. (Amended) A compound of formula (IV)



(IV)

where $R^2$ is H or a protecting group,

$R^3$ is H or a protecting group compatible with $R^2$, and

B is a protected or unprotected heterocyclic base capable of Watson-Crick or Hoogsteen pairing.

17. (Amended) A compound as claimed in Claim 15, wherein B is a protected or unprotected nucleobase selected from adenine, cytosine, guanine, thymine and uracil.

Please add the following claim:

--20. A method of making a compound of formula (V) which method comprises converting a diphenylmethyl ester of N-t-butyoxycarbonyl-cis-r-hydroxy-D-proline by a Mitsunobu reaction in the presence of formic acid to give an inverted formate ester which

is aminolysed to provide the diphenylmethyl ester of N-t-butoxycarbonyl-trans-4-hydroxy-D-proline (V).--

## REMARKS

The present application is being amended in order to recite the cross-reference to prior application 09/284,179, which is a §371 of International Application No. PCT/GB97/02820.

The paragraph on pp. 17-18 has been amended to be consistent with the "Sequence Listing".

Claim 17 has been amended to delete reference to multiple dependent claims. New claim 20 has been added. A marked-up copy of the specification and claim amendments is attached.

Early consideration and allowance of claims 15-18 and 20 are respectfully requested.

Respectfully submitted,

Gordon Lowe

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CFK/FAM/fap

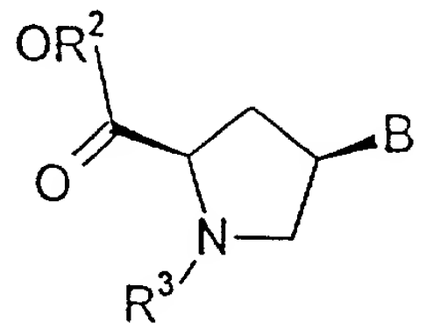
Application No.: Not Yet Known
Examiner: Not Yet Known

**37 CFR §1.121(b)(1)(iii) and (c)(1)(ii)**
**SPECIFICATION AMENDMENTS- MARKED UP VERSION**

At pages 17-18, please replace the paragraph starting at line 29 on page 17 with the following replacement paragraph:

All four bases found in DNA were introduced into the glycylproline building units with the *cis*-D configuration and from these mixed cPNAs containing all four nucleobases have been made. The sequence GTAGATCACT, capped at its C-terminus with L-lysinamide was synthesized, and its binding properties with oligonucleotides investigated. Since it is important to determine the preferred orientation of binding of these novel CPNAs to oligonucleotides, both of the possible complementary oligonucleotides were prepared, *i.e.* [5'-CATCTAGTGA-3'] Sequence ID No. 2, and [5'-AGTGATCTAC-3'] Sequence ID No. 3, and hybridised with the chiral PNA. Their $T_m$ values were 47°C and 43°C respectively indicating that the N-terminus of the cPNA preferentially binds to the 5'-terminus of the olignucleotide, and the C-terminus to the 3'-terminus of the oligonucelotide. This is known as the antiparallel mode of binding, but it is seen that the stability of the alternative parallel binding complex is only slightly less stable.

15. (Amended) A compound of formula (IV)




(IV)

where $R^2$ is H or a protecting group,
$R^3$ is H or a protecting group compatible with $R^2$, and
B is a protected or unprotected heterocyclic base[.] capable of Watson-Crick or Hoogsteen pairing.

17. (Amended) A compound as claimed in Claim 15 [or claim 16], wherein B is a protected or unprotected nucleobase selected from adenine, cytosine, guanine, thymine and uracil.